IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GILEAD SCIENCES, INC., GILEAD PHARMASSET LLC and GILEAD SCIENCES LIMITED, Plaintiffs, Defendants, and Counterclaim Plaintiffs, v. ABBVIE INC., Defendant, Plaintiff and Counterclaim Defendant.	C.A. No. 13-2034 (GMS) (Consolidated with C.A. Nos. 14-209, 14-379)
ABBVIE INC. and ABBVIE IRELAND UNLIMITED COMPANY, Counterclaim Plaintiffs, v. GILEAD SCIENCES, INC., GILEAD PHARMASSET LLC, and GILEAD SCIENCES IRELAND UNLIMITED COMPANY, Counterclaim Defendants.	

OPENING CLAIM CONSTRUCTION BRIEF OF ABBVIE INC.
AND ABBVIE IRELAND UNLIMITED COMPANY

MORRIS, NICHOLS, ARSHT & TUNNELL LLP
Mary B. Graham (#2256)
Derek J. Fahnestock (#4705)
Stephen J. Kraftschik (#5623)
1201 N. Market Street
P.O. Box 1347
Wilmington, DE 19899-1347
(302) 658-9200
mgraham@mnat.com
dfahnestock@mnat.com
skraftschik@mnat.com
Attorneys for AbbVie Inc. and AbbVie Ireland Unlimited Company

OF COUNSEL:

Michael A. Morin
David P. Frazier
Casey L. Dwyer
LATHAM & WATKINS LLP
555 Eleventh Street, NW, Suite 1000
Washington, D.C. 20004-1304
(202) 637-2200

Roger J. Chin
Gregory K. Sobolski
LATHAM & WATKINS LLP
505 Montgomery Street, Suite 200
San Francisco, CA 94111
(415) 391-0600

Gabriel S. Gross
LATHAM & WATKINS LLP
140 Scott Drive
Menlo Park, CA 94025
(650) 328-4600

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NATURE AND STAGE OF THE PROCEEDINGS

AbbVie's allegations in this action are based on, *inter alia*, Gilead's manufacture, use, sale, and offer for sale of Gilead's Harvoni® product for the treatment of Hepatitis C Virus ("HCV") genotype 1 infection, which induces infringement of the Patents-in-Suit. Pursuant to the Court's January 29, 2015 Scheduling Order, AbbVie submits this opening claim construction brief and the accompanying Declaration of Michael Epstein, M.D., a physician with 25 years of experience in the clinical care of patients suffering from HCV infection.[1]

SUMMARY OF THE CLAIM CONSTRUCTION DISPUTES

The parties dispute the construction of two terms that appear in each of the asserted claims. Independent Claim 13 of the '159 patent is representative for claim construction purposes:

> 13. A method of **treatment for HCV**, comprising administering at least two direct acting antiviral agents (DAAs) and ribavirin to an HCV patient infected with HCV genotype 1, wherein said treatment does not include administration of interferon to said patient, wherein said at least two DAAs comprise PSI-7977 and GS-5885, and wherein **said treatment lasts for 12 weeks**.

(A87.) The other asserted claims recite that "said treatment lasts for 8 weeks," (A256, claims 6–11; A343, claims 6–11; A429, claims 1, 3–4) or "said treatment lasts for 8, 9, 10, 11 or 12 weeks," (A256–57, claims 12, 17–20; A343, claims 12, 17–20).[2]

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[1] AbbVie submits Dr. Epstein's Declaration (attached as Exhibit 1) regarding the ordinary meaning of the disputed terms in the relevant field independent of, and complementary to, the intrinsic evidence. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 841 (2015). All emphasis is added unless stated otherwise. Citations in the form "A__" are to pages of the parties' Joint Appendix of Intrinsic Evidence.

[2] For brevity, this brief discusses the intrinsic record of the '159 patent and includes parallel citations to the intrinsic record of the '386 patent. The Patents-in-Suit belong to two families: the '159 patent is representative of one (including the '106 patent), and the '386 patent is representative of the other (including the '984 and '265 patents). The intrinsic record of the '159 and '386 patents inform the proper claim construction of the Patents-in-Suit from their respective families. *See Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1350 (Fed. Cir. 2004).

The parties propose the following constructions of "treatment for HCV" and "said treatment lasts for 12 weeks"[3]:

AbbVie's Proposed Construction	Gilead's Proposed Construction
"medical care to achieve significant efficacy against HCV, as may be measured by sustained virological response (SVR), where the duration is 12 weeks and no longer"	"give for the purpose of stopping or slowing the progression of HCV"; "DAAs are given to a patient for 12 weeks"[4]

There are two disputes. First, AbbVie proposes that "treatment for HCV" does not mean merely slowing or stopping the progression of the virus, but instead requires completely eradicating the virus from the body. That eradication may be determined using a routine measure that appears throughout the intrinsic record, called "sustained virological response," which is the amount of virus in a patient's blood at a certain period after the end of therapy. Eradication is critical because, as repeatedly stated in the intrinsic record, the amount of HCV in a patient's blood can be temporarily suppressed, only to rebound after the end of therapy, thereby prolonging the infection. Second, AbbVie proposes that said treatment "lasts" 8 to 12 weeks, and thus excludes longer durations.

STATEMENT OF FACTS

A. Overview Of HCV Infection

Hepatitis C is a devastating disease of the liver affecting millions of people worldwide. (A32 at 1:29–30; A119 at 1:29–30; *see also* Epstein ¶¶ 5–6.) Chronic HCV infection can lead to life-threatening conditions, including liver disease, liver cancer, and even death. (*Id.*) Although

3 The parties have offered corresponding proposals for asserted claims that recite "said treatment lasts for 8 weeks" or "said treatment lasts for 8, 9, 10, 11 or 12 weeks."

4 Gilead "does not agree that the treatment duration terms, *e.g.*, 'treatment lasts for 12 weeks' should be construed to mean that the treatment lasts for the claimed period of time 'and no longer' as AbbVie has proposed." (7/22/15 Coletti email to Dwyer.) As explained below, Gilead's position contradicts the intrinsic record and the plain meaning of "treatment for HCV" in the context of the Patents-in-Suit.

HCV exists in at least six distinct genetic forms called "genotypes," genotype 1 is the most prevalent in the United States, and the most challenging to treat. (Epstein ¶ 7.)

Curing HCV infection (including genotype 1) has historically been a great challenge. In the prior art, when a patient infected with HCV underwent medical therapy, the level of virus detectable in her blood might be reduced, or even undetectable, for a period—only to subsequently rebound, a phenomenon sometimes called "breakthrough." (A1901 ¶ 3; A2579 ¶ 3); *see also* Epstein ¶¶ 11–13.) Viral breakthrough in turn leads to prolonged infection and continued viral damage. (*Id.*) Thus, a central consideration in the development of regimens for HCV (including genotype 1) infection has been not merely to suppress the amount of virus in the blood, but rather to completely eradicate it from the body. (*Id.*)

To assess whether a regimen actually treats and cures HCV infection, physicians commonly look to a measure called sustained virological response ("SVR"). (A45 at 27:52–56; A132 at 27:8–13; *see also* Epstein ¶ 14.) SVR means that the virus is undetectable in the blood at the end of therapy and also for a sustained period thereafter. (*Id.*) For example, patients who maintain SVR (*i.e.*, no detectable virus) for 12 weeks after therapy are said to have achieved SVR12. As the Patents-in-Suit explain, the SVR rate at 12 weeks after the end of treatment is often "used to express the effectiveness of the present methods of HCV treatment." (A1901 ¶ 3; A2579 ¶ 3; A45 at 27:38–39, 27:52–54; A131 at 26:62–63; A132 at 27:8–11; *see also* Epstein ¶ 15.) And SVR24 "is often considered as a functional definition of cure" for HCV infection. (A45 at 27:60–63; A132 at 27:17–20; *see also* Epstein ¶ 15.)

B. Prior Art HCV Regimens

Prior to AbbVie's patented inventions, the standard of care in the medical community for the treatment of HCV genotype 1 was completely inadequate. Patients endured a grueling long-term regimen that lasted 6–12 months, consisting of weekly injections of a drug called interferon, which produced severe and debilitating side effects, including flu-like symptoms, anemia, cardiovascular events, and psychiatric problems, as well as a drug called ribavirin. (A32 at 1:31–36; A44 at 26:23–53, 26:60–65; A119 at 1:31–36; A131 at 25:47–60, 25:65–26:7; *see also* Epstein ¶¶ 17–18.) Side effects were so severe that many patients could not, or would not, complete therapy. In addition, the prior art regimen was effective in fewer than half of HCV genotype 1 patients. (A44 at 26:53–57; A131 at 25:60–64; *see also* Epstein ¶ 19.) Patients suffering from HCV genotype 1 infection were in a dire situation, facing potential life-long affliction with a progressively debilitating and communicable disease. (Epstein ¶¶ 17–19.)

C. AbbVie's Development Of New Methods Of Treatment For HCV Genotype 1

AbbVie set out to fundamentally change the treatment of HCV genotype 1. AbbVie had spent years successfully developing leading drugs for the treatment of HIV, and brought that vast experience to bear on the challenges of HCV treatment. To meet its goal, AbbVie assembled a multidisciplinary team consisting of physician-scientists versed in preclinical and clinical drug development, including scientists versed in computer modeling of drug effects. The AbbVie team undertook a formidable challenge: to develop a shorter treatment regimen for HCV genotype 1 that would spare patients the debilitating side effects of interferon.

AbbVie's goal stood in stark contrast to the expectations and beliefs of the medical community. (A1811–19; A2567–74) The widespread belief was that patients infected with HCV genotype 1 could not be treated using a short-duration, interferon-free regimen. (*Id.*; A46 at 29:35–38; A132 at 28:57–60.)

AbbVie persevered and succeeded to fundamentally alter the standard of care in HCV genotype 1 treatment. AbbVie developed proprietary drugs called direct acting antiviral agents ("DAA"), a class of drugs that act on various viral components to directly interfere with the HCV life cycle. AbbVie performed pioneering clinical studies using its DAAs in interferon-free, short duration regimens. AbbVie leveraged the insights from its clinical investigations to develop and validate a sophisticated computer model. That model could simulate clinical trial outcomes for short duration, interferon-free combinations of not just AbbVie's proprietary DAAs, but also those developed by other companies.

On October 21, 2011, AbbVie filed the first two provisional U.S. patent applications that ultimately led to the Patents-in-Suit. The Patents-in-Suit all contain claims directed to a method of treatment for HCV genotype 1, using specific combinations of DAAs, without interferon, for short durations lasting only between 8 to 12 weeks.

D. The Claimed Methods Of Treatment

As evidenced throughout the intrinsic record, the inventions of the Patents-in-Suit surprisingly solved the challenges of prior art regimens. AbbVie was the first to develop, and patent, a pioneering method of treatment that included four key features: (i) treatment of HCV genotype 1 (the hardest to treat genotype); (ii) using a combination of two or more DAAs; (iii) without interferon; and (iv) in a short duration lasting no longer than 12 weeks. (A32 at 1:41–45, 1:50–54; A45 at 27:4–13; A119 at 1:41–45, 1:53–57; A131 at 26:28–38.)

AbbVie showed—in actual clinical trial settings—that interferon-free DAA combination regimens could be administered to patients suffering from HCV genotype 1 infection for the short duration of 8 to 12 weeks, eradicating the virus from the body even after the end of that regimen. (A76 at 89:21–29 (10 patients achieving SVR12 and SVR24), *id.* at 90:21–43 (17 patients achieving SVR12 and SVR24), *id.* at 90:56–61 (13 patients achieving SVR12 and 12 patients achieving SVR24); A77 at 91:56–92:10 (10 patients achieving SVR8); A78 at 93:1–11 (5 patients achieving SVR8), *id.* at 94:20–30 (6 patients achieving SVR12), *id.* at 93:31–44 (9 patients achieving SVR12).)

AbbVie also developed a path-breaking proprietary computer model capable of evaluating optimal doses and durations of interferon-free, DAA combination therapies for HCV genotype 1. (A82 at 101:37–47; A165 at 94:34–44.) AbbVie's model could simulate clinical trial outcomes of short duration, interferon-free, DAA combination regimens, and predict whether a regimen was clinically effective in subjects infected with HCV genotype 1. (A78 at 93:25–27; A82 at 101:45–54; A165 at 94:14–17, 94:41–50.)

From these efforts, AbbVie learned that certain short duration, interferon-free, DAA combination therapies could be clinically effective against HCV genotype 1 infection. The Patents-in-Suit disclose as much. (A32–38 at 2:31–14:35; A36–37 at 10:53–11:2; A37 at 11:11–13, 11:19–39, 11:45–47; A119–25 at 2:34–14:21; A123 at 10:39–55, 10:64–65; A124 at 11:5–23, 11:31–33.) The claims of the Patents-in-Suit in turn include interferon-free, short duration, DAA combination regimens that treat HCV genotype 1. Those claims include using the combination of PSI-7977 and GS-5885, which Gilead years later marketed as Harvoni®, an interferon-free, short duration therapy for the treatment of HCV genotype 1 infection.

One key aspect of the claimed inventions is the development of methods that are effective —*i.e.*, they actually eradicate HCV genotype 1 from the body. The specification explains "in the methods, at least two DAAs and ribavirin are administered *in effective amounts* to provide a desired *measure of effectiveness* in the subject." (A45 at 27:32–35; *see also* A131 at 26:57–60.)

The specification further states that "[v]arious measures may be used to express the effectiveness of the present methods of HCV treatment." (A45 at 27:38–39; A131 at 26:62–63.) But while multiple metrics can be used throughout the process, long-term efficacy is measured by "(SVR), which, as used herein, means that the virus is undetectable at the end of therapy," and, a sustained duration thereafter, "preferably, the virus is undetectable at the end of therapy and for at least 12 weeks after the end of therapy (SVR12) . . . .” (A45 at 27:52–56; A132 at 27:8–13.) Achieving SVR in an interferon-free, DAA combination regimen lasting no more than 12 weeks was unexpected and surprising. (A46 at 29:35–38, 29:45–53; A132–33 at 28:57–60, 28:64–29:6.)

Another key aspect of the claimed inventions is eradicating HCV genotype 1 infection using a 12 week duration of treatment and no longer. For example, the specification discloses that “[i]t was unexpectedly discovered that an interferon-free treatment using a combination of two or more DAAs, together with ribavirin, and for a *duration of no more than 12 weeks, could achieve significant SVR*.” (A46 at 29:35–38; *see also* A132 at 28:57–60.) As another example, the specification discloses “[t]herapeutic agent 1 and therapeutic agent 2 can be administered in *therapeutically effective amounts to provide a SVR* (for example, a SVR8, SVR12, SVR16, or SVR24) with a *treatment duration of no more than 12 weeks*, preferably no more than 8 weeks.” (A60 at 57:17–22; *see also* A147 at 58:42–47.) The specification further discloses that, “[t]he duration of the treatment regimen is *no more than twelve weeks* (*e.g.*, the duration being 12 weeks; or the duration being 11, 10, 9, 8, 7, 6, 5, 4, or 3 weeks).” (A33 at 4:39–43; A120 at 4:38–41.)

E. The Prosecution Of The Patents-In-Suit

The central focus of AbbVie’s prosecution of the Patents-in-Suit was demonstrating to the Examiner that the claimed methods surprisingly and unexpectedly achieved significant efficacy (such as measured by SVR), within 12 weeks or less, to “treat” HCV genotype 1 infection.

As originally filed, independent claim 1 of the ’159 patent application recited:

> 1. A method of treatment for HCV, comprising administering at least two direct acting antiviral agents (DAAs) and ribavirin to an HCV patient, wherein said treatment does not include

> administration of interferon to said patient, and said treatment lasts for 8, 9, 10, 11 or 12 weeks.

(A608; *see also* A2344.) Dependent claim 18 recited: "The method of claim 1, wherein said at least two DAAs comprise PSI-7977 and GS-5885." (A609; A2345.)

The Examiner rejected claim 1 as anticipated by WO 2010/031832 ("Lin") under 35 U.S.C. § 102(b). (A891–92; A2452–53.) According to the Examiner, Lin disclosed a method of treating HCV comprising two particular DAAs. (A891; A2452.) While the Examiner recognized that Lin did "not provide any instruction that the treatment should be interrupted, or stopped for any reasons," he believed that "the continued treatment for a long period of time, *such as 8 to 12 weeks*, would have been at once envisaged by one of ordinary skill in the art as HCV infection cannot be cured in a short period of time . . . ." (A892; A2453.)

The Examiner also rejected all pending claims as obvious under 35 U.S.C. § 103(a). (A892–96; A2453–57.) He stated that, while Lin did not disclose "particular preference as to the genotypes of treated viral infection" and did "not provide any instruction that the treatment should be interrupted, or stopped for any reason," other references disclosed existence of genotype 1, or the existence of various DAAs. (*Id.*)

Applicants held an interview with the Examiner to discuss the state of the prior art regarding HCV infection. (A1427; A2498.) They pointed out that, contrary to the Examiner's misapprehension of a "long period of treatment," it was "conventional wisdom in the art that 48 weeks are required for HCV treatment." (*Id.*) Thus, Applicants agreed to limit the pending '159 patent claims "to particular combinations and 12 weeks treatment," which was far shorter than the prior art standard of care. (*Id.*) Focusing on the significant efficacy of the claimed methods, they explained that, as amended, the claimed inventions "achieve the results normally achieved by 48 weeks treatments" in that shorter period of time, and that this was "unexpected and unobvious." (*Id.*)

Applicants in turn cancelled claim 1 and presented an amended claim 18 in independent form:

> 18. (currently amended) A method of treatment for HCV, comprising administering at least two direct acting antiviral agents (DAAs) and ribavirin to an HCV patient infected with HCV genotype 1, wherein said treatment does not include administration of interferon to said patient, ~~The method of claim 1,~~ wherein said at least two DAAs comprise PSI-7977 and GS-5885, and wherein said treatment lasts for 12 weeks.

(A1805 (annotations in original); *see also* A2561.) Applicants specified that the claims are directed to the treatment of HCV genotype 1, in particular, by administering a specific DAA combination, without interferon, for no more than 12 weeks.

In connection with their amendments and the Examiner's rejection, Applicants unambiguously clarified the scope of the claimed inventions. They distinguished the prior art for its failure to disclose the clinical efficacy of the claimed inventions. In particular, Applicants stated: "The Office Action does not explain, and cannot explain, why any DAA combinations described in the cited references would be indicative of *the effectiveness* of the DAA combinations recited *in the present claims.* Indeed, as demonstrated below, certain DAA combinations *did not work*." (A1809; A2565.)

Applicants further emphasized achieving significant efficacy within a short duration. They stated that "none of the cited references suggests that any DAA combination would likely *work* in a *12-week*, interferon-free treatment regimen *for HCV genotype 1*. As appreciated by one skilled in the art, *in vitro* assays or dose response curves are *not sufficient to show the effectiveness of a HCV treatment.*" (*Id.*)

Applicants then clearly explained how to understand whether an HCV genotype 1 treatment "works" in the context of the claimed inventions:

> Instead, *one of ordinary skill in the art would use the sustained viral response (SVR) as a measure to determine whether a HCV treatment works or not. See* paragraph 3 of Dr. Podsadecki Declaration (Exhibit 1). SVR is defined as the absence of detectable HCV RNA in blood serum *after completing the treatment*.

(*Id.*; *see also* A1810; A2566 ("whether a HCV treatment works or not is measured by the SVR rates").) In other words, Applicants pointed out that achieving SVR was the proper measure of "treatment," in contrast to merely suppressing viral load temporarily while the drug was administered, which may not be indicative of sustainably eliminating HCV.

Applicants referred the Examiner to clinical data from a single-DAA study in a difficult to treat population, in which PSI-7977 and ribavirin were administered for 12 weeks (and no longer), without interferon, to subjects infected with HCV genotype 1. (A1809–10; A2565–66.) Applicants explained that, in the study, HCV viral load was "quickly suppressed," and was undetectable "[w]ithin about 3 weeks" after the start of the regimen. (*Id.*) Yet, they explained, "*after the completion of the 12-week treatment*, the HCV RNA levels in most patients almost immediately *rebounded, leading to treatment failure*." (A1810; A2566.) Applicants subsequently contrasted such results against those presented in a March 2013 study of the combination of PSI-7977 and GS-5885, which "achieved 100% SVR_{12} after 12-week, interferon-free treatment for HCV genotype 1." (A2010; A2764.)

Applicants further explained that the prior art taught away from administering interferon-free DAA combinations for no more than 12 weeks to treat HCV genotype 1. (A1811–13; A2567–69.) They discussed a clinical study that attempted to administer an interferon-free, two-DAA combination for 12 weeks to subjects infected with HCV genotype 1, but which "had to be stopped due to on-treatment *viral breakthroughs*"—*i.e.*, rebound. (A1811; A2567.) Against this state of the prior art, Applicants demonstrated that the achievement of significant efficacy of the claimed inventions was a fundamentally surprising and unexpected result. (*See* A1814–18; A2570–74.)

In support, Applicants submitted the declaration of named co-inventor, Dr. Thomas Podsadecki, a physician with experience in the clinical development of HCV drugs. He explained that, "HCV virus has been known to be prone to *rebound* after the completion of a treatment *despite a seemingly successful suppression* during the treatment." (A1901 ¶ 3; A2579 ¶ 3.) "As a result," he added, "one of ordinary skill in the art would use the *sustained viral response (SVR) as a measure to determine whether a HCV treatment works or not* . . . ." (*Id.*)

Dr. Podsadecki also explained the unexpected and surprising result of achieving SVR in the claimed invention in light of the prior art standard of care for HCV genotype 1. (*Id.* ¶ 4.) He emphasized that, prior to October 2011, there was "no clinical data showing any *successful treatment* for HCV genotype 1 using only DAAs without interferon in a 12-week regimen." (*Id.* ¶ 6.)

The Examiner "fully considered" Applicants' amendments and remarks regarding how to ascertain the success of the claimed method of treatment. (A2101; A2823.) He found them "persuasive" and agreed that the prior art did not "teach or fairly suggest the *12-week interferon-free treatment* of HCV genotype 1 with the particular combination herein *and its unexpected success* as shown in the application, as well as the exhibits presented herein." (A2099 ¶ 3; A2824 ¶ 3.)

ARGUMENT

I. Legal Standard

"[T]he words of a claim 'are generally given their ordinary and customary meaning.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Where claim construction involves technical terms in a scientific field, determining the ordinary and customary meaning of the disputed term "requires examination of terms that have a particular meaning in a field of art." *Id.* In such instances, "the court looks to 'those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean,' . . . includ[ing] 'the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art.'" *Id.* (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

II. "Treatment for HCV" / "Said Treatment Lasts for 12 Weeks"

A. The Evidence Supports AbbVie's Proposed Construction

AbbVie's proposed construction accurately reflects how the Patentees used the disputed terms throughout the intrinsic record. Throughout the specification and prosecution, the Patentees made express and persistent statements that, in the context of the claimed invention, a "treatment for HCV" that "lasts" for 8 to 12 weeks refers to medical care that eradicates the virus from the body, which in turn permits the treatment duration to be 8 to 12 weeks and no longer. Independent of, and complementary to, the intrinsic evidence, Dr. Epstein provides foundational background on HCV infection and how those in the field think about its treatment and duration of therapy. Dr. Epstein also explains his belief that AbbVie's construction reflects common usage of treatment and duration in the field.[5]

1. The Claim Language

By its plain language, Claim 13 of the '159 patent (A87) (and the other asserted claims) refers to not merely "a method of treatment," but rather a method of treatment that is "for HCV" genotype 1 infection and "lasts 12 weeks." In the particular context of treating HCV, one of ordinary skill understands that HCV genotype 1 infection has unique clinical considerations. (*See* p. 3, *supra*; Epstein ¶¶ 25–26.) Among them is that HCV genotype 1 infection is not treated—and cannot be cured—until the regimen achieves a sustained period of viral eradication. (*Id.*) Thus, by reciting that the treatment "lasts" for 12 weeks, Claim 13 of the '159 patent indicates to one of ordinary skill that such a duration is effective for sustained viral response. No further duration is warranted.

Moreover, the plain language of the asserted claims, as well as common sense, confirms that "lasts" does not mean "at least," as Gilead suggests. For example, certain asserted claims recite "said treatment lasts for 8, 9, 10, 11 or 12 weeks." (A256–57, claims 12, 17–20; A343, claims 12, 17–20.) If Gilead's proposal that "lasts X weeks" means "*at least X weeks*," then reciting "9, 10, 11 or 12 weeks" in these claims would be superfluous. Quite simply, if Gilead were correct, then as a matter of grammar, "lasts for 8 weeks" would cover 9–12 weeks (and longer). But that would render the express claim language of "9, 10, 11 or 12 weeks" superfluous, "contrary to the well-established rule that 'claims are interpreted with an eye toward giving effect to all terms in the claim.'" *Digital-Vending Servs. Int'l, LLC v. Univ. of Phoenix, Inc.*, 672 F.3d 1270, 1275 (Fed. Cir. 2012) (internal citation omitted). By contrast, under

[5] AbbVie's discussion of the ordinary meaning of the claim terms draws on the understanding of a clinician with experience treating patients infected with HCV. Such expertise is within the level of ordinary skill in the art. (*See, e.g.*, A32 at 1:14–15, 1:29–36; A75 at 87:34–37.)

AbbVie's construction, all of the claim language has full effect—"said treatment lasts for X weeks" means the treatment duration is X weeks, no more and no less.

2. The Specification

The specification of the '159 patent consistently discloses that, in the context of the claimed invention, "treatment" for HCV genotype 1 refers to medical care that achieves significant long-term efficacy in the patient with a short-duration therapy. (*See* pp. 5–7, *supra*.) For example, the "Brief Summary of the Invention" discloses that "the two or more [DAAs] and ribavirin are administered in amounts *effective to provide a sustained virological response (SVR)* or achieve another desired *measure of effectiveness* in a subject" within 12 weeks or less, (A32 at 1:46–50; *see also* A119 at 1:46–50), and goes on to explain that, "[i]n the foregoing methods as well as methods described herein, the DAAs and ribavirin can be administered in any *effective* dosing schemes . . . ." (A32 at 2:62–64; A45 at 27:4–13; *see also* A119 at 2:65–67; A131 at 26:28–38.) The specification's focus on clinical efficacy, achieved within a duration that is no longer than 12 weeks, applies in particular to the combination of PSI-7977 and GS-5885, the two DAAs recited in Clam 13 of the '159 patent. (*See, e.g.*, A36–37 at 10:53–11:2, 11:11–13; A123 at 10:64–65 ("the patient being treated can be infected with HCV genotype 1").)

The specification discloses various measures of the clinical efficacy of the claimed treatment regimens. (*See* A45 at 27:38–67; A131–32, 26:62–27:24; *see also* Epstein ¶ 27.) Among them, the measure of long-term sustained eradication is SVR. (*See* A45 at 27:52–67, A19–31; A132 at 27:8–24; A106–18; Epstein ¶ 27.) The specification discloses the latter as a measure of whether a regimen for HCV genotype 1 infection is in fact a "treatment." (*Id.*)

3. The Prosecution History

The prosecution history of the '159 patent likewise contains express statements by the Patentees that the claimed "treatment for HCV" genotype 1 that "lasts for 12 weeks" is one in which the medical care achieves significant efficacy against the infection, as measured by a sustain viral response within 12 weeks—and no longer—of starting the regimen. (*See* pp. 8–12, *supra*.) Where, throughout prosecution, the "inventors have consistently relied on [claim limitations at issue] as the dividing line" between the invention and prior art, that is particularly instructive of the proper claim construction. *Takeda Pharm. Co. v. Zydus Pharm. USA, Inc.*, 743 F.3d 1359, 1365 (Fed. Cir. 2014).

As an initial matter, as originally filed, the claims of the '159 patent application did not recite that the claimed method for treatment of HCV was specifically for "genotype 1" or that the claimed treatment "lasts for 12 weeks" only. (A608; A2344.) In response to the Examiner's non-final rejection of those claims, however, Applicants added those limitations to the pending claims. (A1803–06; A2559–62.)

In connection with that amendment, Applicants explained that the claimed invention could achieve within only 12 weeks the "the results normally achieved by 48 weeks treatments." (A2498; A1427; *see also* Epstein ¶¶ 28–31.) The "results" at issue referred to the prior art standard of care for interferon-containing regimens, which achieved sustained virological response—not merely some decrease in viral load—albeit using a much more burdensome regimen with a much longer duration necessary to achieve treatment.

In light of these claim amendments, Applicants explained why the Examiner's rejections should be overcome. They distinguished the cited prior art on the basis of "*the effectiveness* of the DAA combinations recited *in the present claims*," emphasizing various prior art DAA combinations that "did not work" or would not "likely work" in a 12-week, interferon-free regimen. (A1809; A2565; *see also* Epstein ¶¶ 28–31.)

Moreover, Applicants clarified how they understood the claimed method of treatment to "work" in the context of treating HCV genotype 1. They explained that a person of ordinary skill "would use the *sustained viral response (SVR) as a measure to determine whether a HCV treatment works or not*," and echoed the specification's definition of SVR as "the absence of detectable HCV RNA in blood serum *after completing the treatment*." (*Id.*)

After establishing SVR as a key measure of the claimed method of treatment, Applicants used it to distinguish the prior art and explain why the invention's achievement of significant efficacy in an interferon-free, DAA combination regimen lasting 12 weeks or less was surprising and unexpected. In particular, they apprised the Examiner of an existing study involving a 12-week, interferon-free DAA regimen. In that study, they explained, though HCV viral load "quickly suppressed" and was even "undetectable" within just 3 weeks, "*after the completion of the 12-week treatment*, the HCV RNA levels in most patients almost immediately rebounded**,** leading to *treatment failure*." (A1810; A2566.)

Quite simply, Applicants made clear that, for purposes of the claims, the proper measure of efficacy is not simply achieving viral suppression, but rather achieving eradication within the 12 week duration of the regimen, as confirmed by SVR.

The Podsadecki Declaration supported Applicants' response to the Examiner. Dr. Podsadecki described that, in the context of HCV genotype 1 infection, there might be a "seemingly successful suppression" that nonetheless did not constitute a treatment "that works" for its failure to achieve "effectiveness" as a "treatment." (A1901 ¶ 3; A2579 ¶ 3; *see also* Epstein ¶ 32.) He then explained that, in the field of HCV treatment, a common measure of clinical efficacy is SVR at the end of the duration period. Dr. Podsadecki further acknowledged prior art interferon-free DAA combination therapies, but distinguished them from the claimed invention on the grounds that none of these amounted to data showing "successful treatment for HCV genotype 1" in an interferon-free regimen limited to 12 weeks in duration. (*Id.* ¶¶ 4–5.)

The Examiner agreed with Applicants' statements about the standard of care, assessment of whether treatment "works" by reference to its "effectiveness," and related grounds for distinguishing the claimed invention from the prior art. (A2101; A2823; A2099 ¶ 3; A2824 ¶ 3.) The Examiner's agreement is a further indication in the intrinsic record that Applicants intended the claimed invention to encompass the achievement of significant clinical efficacy within 12 weeks (as well as 8, 9, 10 or 11 weeks).

4. The Extrinsic Evidence

While the intrinsic record alone supports AbbVie's proposed construction, Dr. Epstein explains (just as the intrinsic record does) that clinicians who care for patients suffering from HCV genotype 1 infection understand the problem of viral rebound and continuing viral damage following some viral suppression. (Epstein ¶¶ 11–13.) Accordingly, Dr. Epstein explains, in this field, "treatment" is widely understood to require a measure of sustained eradication to indicate significant efficacy. (*Id.* ¶¶ 14–16.) As in the intrinsic record, SVR is a common metric of such efficacy. (*Id.* ¶ 15.) In light of that understanding, in this field, the duration of "treatment" refers to the point at which SVR is achieved. (*Id.* ¶¶ 28–33.) At that point, there is by definition sustained eradication of the virus, and thus the treatment lasts no longer than the prescribed duration. (*Id.*)

B. The Evidence Contradicts Gilead's Proposed Construction

Gilead's proposal contradicts the intrinsic record in two fundamental ways. First, it ignores Applicants' repeated statements to the Examiner that stopping or slowing the progression of the virus without complete eradication is not "treatment" of HCV genotype 1. Indeed, nothing in the patent specification suggests that something other than eradication of the virus would "slow progression" of the disease. (*See also* Epstein ¶¶ 34–36.)

Second, Gilead's proposal ignores that, in the context of the claimed method of treatment, the reference to a 8, 9, 10, 11, or 12-week treatment reflects the unexpected surprising result that SVR could be achieved within those durations—and no more—as compared to the prior art standard of care lasting 24 to 48 weeks. In keeping with the prosecution history (*see* p. 8–9, *supra*), the specification repeatedly discloses embodiments in which the duration of treatment is "no more than 12 weeks." (*See, e.g.*, A32 at 2:13–14; A33 at 4:7–8, 39–42; A35 at 8:28–31; A36 at 9:57–60, 10:28–31, 10:62–65; A37 at 11:28–31, 11:62–65, 12:23–26; A38 at 13:31–34; A119 at 2:16; A120 at 4:6–7, 38–41; A122 at 8:14–17; A123 at 10:49–52; A124 at 11:14–17; A131 at 26:28–38; A132 at 28:57–60.)

Gilead's proposed construction of "treatment" in this case contradicts positions regarding a virological disease it successfully argued before another district court. In *Gilead Sciences, Inc. v. Mylan Inc.*, the claim at issue was directed to methods of treating HIV infection using fixed dose combination formulations of two drugs. C.A. No. 1:14-cv-99, 2015 WL 2238060, at *11–12 (N.D. W. Va. May 12, 2015). The parties disputed the ordinary meaning of "*treatment* of the symptoms or effects of an HIV infection." *Id.* at *11. Gilead proposed to construe the limitation to mean "treatment of the symptoms or effects of an HIV infection *that is therapeutically effective*." *Id.* at *11. By contrast, Mylan proposed to construe the term as "treatment of the symptoms or effects of an HIV infection *to any extent*." *Id.*

Gilead's supporting arguments were illuminating with respect to the present issue. Gilead emphasized that its construction was "consistent with the patentees' intent to provide a *therapeutically effective* method of treating HIV," as "reflected throughout the express language of the specifications and prosecution histories." (Ex. 2 at 3, *see also id.* at 17–19.) As the court observed, Gilead pointed to "repeated references to 'therapy' and 'therapeutic combinations'" in the specifications at issue in order "to establish that the inventors intended their treatment to be 'therapeutically effective.'" *Gilead Scis.*, 2015 WL 2238060 at *13. Likewise here, the specification repeatedly discloses that the method of treatment achieves significant efficacy (*e.g.*, SVR12) within a short duration of 12 weeks or less. Gilead also argued that "the prosecution histories . . . clarify that treatment must be 'effective,' particularly since HIV is a chronic and life-threatening disease, requiring long-term treatment with anti-viral medications.'" *Id.* at *14. Likewise here, the prosecution history clarifies that treatment for HCV, including genotype 1, must be significantly effective, particularly because HCV infection is chronic and the virus is known to rebound even after a period of viral suppression.

The court in *Gilead Sciences* agreed that the prosecution history "demonstrates that the inventors knew the difference between effective and ineffective treatment, having relied upon the fact that their treatment was effective to distinguish it from the prior art." *Id.* at *15. Likewise here, the prosecution history demonstrates that the inventors knew the difference between mere viral suppression and eradication, as demonstrated by SVR. Gilead's proposed construction to the contrary cannot be reconciled against that evidence.

Gilead relied on a declaration from a clinician with expertise in HIV infection. (*See* Ex. 3.) He explained that "the definition of 'treatment of the symptoms or effects of an HIV infection' *should be limited to treatments that are clinically meaningful or therapeutically effective*," as opposed to treatments "to any extent." (*Id.* at ¶¶ 21–22.) Gilead relied on that extrinsic evidence to argue that "[d]octors would only consider a particular drug regimen to 'treat' an HIV-infected patient *if it produces a meaningful drop* in HIV viral load," emphasizing the "clinical reality" that, in the context of the claimed invention, treatment meant "clinically meaningful or therapeutically effective treatments." (Ex. 2 at 20.) And the court agreed that the "intrinsic and extrinsic evidence are consistent" in adopting Gilead's construction. *Gilead Scis.*, 2015 WL 2238060, at *17. This is AbbVie's position, supported by Dr. Epstein's declaration. In the context of HCV genotype 1 infection, physicians would only consider "treatment" to refer to achieving complete viral eradication, such as measured by SVR, within the treatment duration.

CONCLUSION

For the foregoing reasons, AbbVie asks that the Court adopt its proposed construction of the disputed claim language.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Mary B. Graham

Mary B. Graham (#2256)
Derek J. Fahnestock (#4705)
Stephen J. Kraftschik (#5623)
1201 N. Market Street
P.O. Box 1347
Wilmington, DE 19899-1347
(302) 658-9200
mgraham@mnat.com
dfahnestock@mnat.com
skraftschik@mnat.com
Attorneys for AbbVie Inc. and AbbVie Ireland Unlimited Company

OF COUNSEL:

Michael A. Morin
David P. Frazier
Casey L. Dwyer
LATHAM & WATKINS LLP
555 Eleventh Street, NW, Suite 1000
Washington, D.C. 20004-1304
(202) 637-2200

Roger J. Chin
Gregory K. Sobolski
LATHAM & WATKINS LLP
505 Montgomery Street, Suite 200
San Francisco, CA 94111
(415) 391-0600

Gabriel S. Gross
LATHAM & WATKINS LLP
140 Scott Drive
Menlo Park, CA 94025
(650) 328-4600

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